57 PERIPHERAL NEUROPATHY

General Discussion

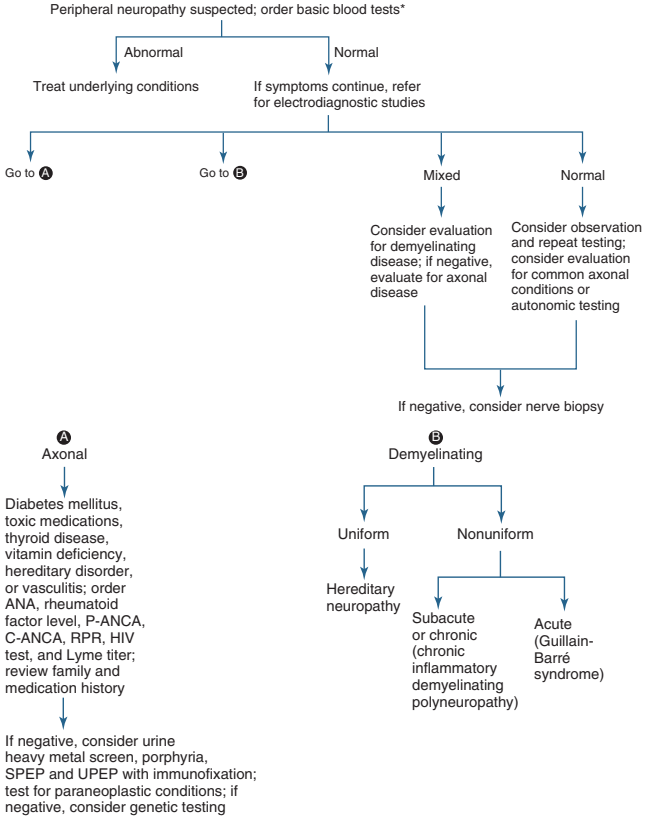
Peripheral neuropathy represents one of the most common neurologic disorders encountered by primary care physicians. The term *peripheral neuropathy* is usually used to describe symmetric and universal damage to adjacent nerves. The damage and clinical manifestations usually are located distally with a proximal progression. Peripheral neuropathy may be the result of hereditary, toxic, infectious, inflammatory, metabolic, ischemic, or paraneoplastic causes. Diabetes and alcoholism are the most common etiologies of peripheral neuropathy in adults living in developed countries. It is important to differentiate a true neuropathy from other disorders that can have a similar clinical presentation (Figure 57-1). Despite extensive evaluation, an etiology is not found in 13% to 22% of cases.

The first step in the evaluation is to determine whether the symptoms are the result of a peripheral neuropathy or a lesion in the central nervous system, as well as whether a single nerve root, multiple nerve roots, or a peripheral nerve plexus is involved. Central nervous system lesions may be associated with additional features, such as diplopia, cranial nerve involvement, speech difficulty, or ataxia. Deep tendon reflexes are usually brisk, and muscle tone is spastic. Lesions of the peripheral nerve roots typically are asymmetric, follow a dermatomal pattern of sensory symptoms, and may be associated with neck or low back pain. Lesions of a peripheral nerve plexus are asymmetric with sensorimotor involvement of multiple nerves in one extremity.

Most patients can be diagnosed, classified, and managed based on the history and physical examination. Classifying the patient's neuropathy clinically based upon time course (acute, subacute, chronic, or lifelong), functional modalities affected (motor or sensory), and the distribution (distal, proximal, or patchy) can assist in diagnosis. Other important information includes medication use, medical history, age of onset, and family history.

Medications Associated with Neuropathy

Alfa interferon
Amiodarone
Amitriptyline
Chloramphenicol
Chloroquine
Cimetidine
Cisplatin
Colchicine
Dapsone
Didanosine



**— Complete blood count, comprehensive metabolic panel, and measurement of erythrocyte sedimentation rate and fasting blood glucose, thyroid-stimulating hormone, and vitamin B_{12} levels (possibly with methylmalonic acid and homocysteine levels).*

Figure 57-1 Diagnosis of suspected peripheral neuropathy. (From Azhary H, Farooq MU, Bhanushali M, Majid A, Kassab MY. Peripheral neuropathy: differential diagnosis and management. *American Family Physician* 2010;81:887–892; Figure 1.)

Dideoxycytidine
Dideoxyinosine
Digoxin
Disulfiram
Docetaxel
Ethambutol
Gold

Hydralazine
Isoniazid
Lithium
Metronidazole
Nitrofurantoin
Nitrous oxide
Paclitaxel
Phenytoin
Procainamide
Pyridoxine (vitamin B_6) excess
Statins
Suramin
Thalidomide
Vincristine

Causes of Peripheral Neuropathy

Acute pandysautonomia
Alcoholism
Amyloidosis
Carcinomatous axonal sensorimotor polyneuropathy
Charcot-Marie-Tooth disease
Chronic gluten enteropathy
Chronic inflammatory demyelinating polyradiculopathy
Chronic liver disease
Crohn disease
Churg-Strauss vasculitis
Compressive neuropathies
Critical illness neuropathy
Cryoglobulinemia
Diabetes mellitus
Diphtheria toxin
End-stage renal disease
Entrapment
- Acromegaly
- Amyloidosis
- Myxedema
- Rheumatoid arthritis

Folate deficiency
Friedreich ataxia
Gastric restriction surgery for obesity
Gouty neuropathy
Guillain-Barré syndrome
Hereditary motor sensory neuropathy
Heroin
HIV/AIDS

Hypophosphatemia
Hypothyroidism
Idiopathic sensory neuronopathy
Ischemic lesions
Leprosy
Lyme disease
Lymphoma
Lymphomatous axonal sensorimotor polyneuropathy
Metachromatic leukodystrophy
Metal neuropathy
- Acute arsenic polyneuropathy
- Chronic arsenic intoxication
- Lead neuropathy
- Mercury
- Gold
- Thallium

Monoclonal gammopathy
Monoclonal gammopathy of undetermined significance
Multiple myeloma
Neoplastic infiltration or compression
Organophosphates
Osteosclerotic myeloma
Paraneoplastic neuropathy
Paraproteinemias
Plasmacytoma
Polyarteritis nodosa
Porphyria
Postgastrectomy syndrome
Primary biliary cirrhosis
Refsum disease
Rheumatoid arthritis
Sarcoidosis
Sjögren syndrome
Styrene-induced peripheral neuropathy
Syphilis
Systemic lupus erythematosus
Tetanus
Thiamine deficiency
Tic paralysis
Toxic neuropathy
- Acrylamide
- Carbon disulfide
- Carbon monoxide
- Dichlorophenoxyacetic acid
- Ethylene oxide

- Glue sniffing
- Hexacarbons
- Organophosphorus esters

Trauma
Vasculitis
Vitamin B_6 deficiency
Vitamin B_{12} deficiency
Vitamin E deficiency
Waldenström macroglobulinemia
Whipple disease

Suggested Work-Up

Fasting serum glucose and glycosylated hemoglobin	To evaluate for diabetes mellitus
Alanine aminotransferase and aspartate aminotransferase	To evaluate for occult alcoholism
Comprehensive metabolic panel	To evaluate for metabolic derangement or renal disease
Complete blood count	To evaluate for evidence of infection
Erythrocyte sedimentation rate, antinuclear antibody (ANA), rheumatoid factor	To evaluate for inflammatory and rheumatologic disorders
Urinalysis	To evaluate renal function
Vitamin B_{12} level	To evaluate for pernicious anemia
Thyroid-stimulating hormone level	To evaluate for thyroid abnormalities
Electromyography (EMG) and nerve conduction studies (NCS)	Indicated if the diagnosis remains unclear after initial diagnostic testing. Used to confirm the presence of a neuropathy and provide information regarding the types of fibers involved, the pathophysiology, and a symmetric versus asymmetric or multifocal pattern.

Neurologic consultation should be obtained early for any acute progressive neuropathy. EMG and/or NCS, electrocardiogram, lumbar puncture, chest radiograph, and pulmonary function tests are often performed in patients with acute progressive neuropathy.

Additional Selected Work-Up

Serum and urine protein electrophoresis	To evaluate for paraproteinemic and/or demyelinating neuropathies or multiple myeloma
HIV antibodies	If HIV infection is suspected
Cerebrospinal fluid analysis	Useful in the evaluation of myelinopathies and polyradiculopathies
Angiotensin-converting enzyme level	If sarcoidosis is suspected
Cryoglobulins	If cryoglobulinemia is suspected
Lyme polymerase chain reaction	If Lyme disease is suspected
Rapid plasma reagin (RPR); venereal disease research laboratory (VDRL)	If syphilis is suspected
Urinalysis, including 24-hour collection	If heavy metal toxicity or porphyria is suspected
Antinuclear antibody (ANA); perinuclear anti-neutrophil cytoplasmic antibody (P-ANCA); cytoplasmic anti-nuclear cytoplasmic antibody (C-ANCA)	If vasculitis is suspected
Cytology	If lymphoma is suspected
Nerve biopsy	Used in specific cases to diagnose vasculitis, leprosy, amyloid neuropathy, leukodystrophies, and sarcoidosis
Paraneoplastic panel	If underlying malignancy is suspected
Antisulfatide antibodies	If autoimmune polyneuropathy is suspected
Genetic testing	If hereditary neuropathy is suspected
Salivary flow rate, Shirmer test, rose bengal test	If Sjögren syndrome is suspected

Further Reading

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